Detection of Freezing of Gait in Patients with Parkinson's Disease using Electroencephalography and Computational Intelligence

By

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Certificate of Authorship/Originality

I, Aluysius Maria Ardi Handojoseno, certify that the work in this thesis has not previously been submitted for a degree, nor has it been submitted as part of the requirements of a degree, except as fully acknowledged within the text.

I also certify that this thesis has been written by me. Any help that I have received in my research work and in the preparation of the thesis itself has been acknowledged. In addition, I certify that all information sources and literature used are indicated in the thesis.

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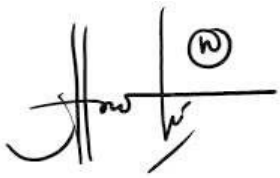

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“Teach us to give and not to count the cost”

St. Ignatius Loyola

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Nomenclature

3D-SSP	:	3-dimensional Stereotactic Surface Projections
AD	:	Alzheimer Disease
ANN	:	Artificial Neural Networks
APSD	:	Auto-Power Spectral Densities
AR	:	Autoregressive
BA	:	Brodmann Area
BSS	:	Blind Source Separation
CPSD	:	Cross Power Spectral Density
CS	:	Centroid Scale
CWT	:	Continuous Wavelet Transform
DALY	:	Disability Adjusted Life Years
dDTF	:	Direct Directed Transfer Function
DNN	:	Dynamic Neural Network
DSM-IV	:	Diagnostic and Statistical Manual of Mental Disorder, Fourth Edition
DTF	:	Directed Transfer Function
DWT	:	Discrete Wavelet Transforms
EEG	:	Electroencephalography
EMG	:	Electromyography
EOG	:	Electrooculography
ffDTF	:	Full Frequency Directed Transfer Function
FFT	:	Fast Fourier Transform
FI	:	Freeze Index
fMRI	:	Function Magnetic Resonance Imaging
FOG	:	Freezing of Gait
FOG-Q	:	Freezing of Gait Questionnaire
H&Y	:	Hoehn and Yahr

ICA	:	Independent Component Analysis
MEG	:	Magnetoencephalography
MGAP	:	Microbe Genome Annotation Platform
MLP-NN	:	Multi Layer Perceptron Neural Networks
MMSE	:	Mini Mental State Examination
MRP	:	Movement-Related potentials
MSC	:	Magnitude Squared Coherence
MVAR	:	Multivariate Autoregressive
NFOG-Q	:	New Freezing of Gait Questionnaire
PCA	:	Principle Components Analysis
Pcc	:	Pearson's Correlation Coefficient
PD	:	Parkinson's Disease
PDC	:	Partial Directed Coherence
PLV	:	Phase Locking Value
PSD	:	Power Spectral Density
PSE	:	Power Spectral Entropy
PWF	:	Patient with PD with FOG
PWoF	:	Patient with PD without FOG
PWP	:	Patient with PD
RAS	:	Rhythmic Auditory Stimulation
ROI	:	Region of Interest
RT	:	Reaction Time
SCF	:	Spectral Centroid Frequency
sGPDC	:	Squared Generalized Partial Directed Coherence
SMA	:	Supplementary Motor Area
SPECT	:	Single Photon Emission Computed Tomography
TUG	:	Timed Up and Go
UPDRS	:	Unified Parkinson's Disease Rating Scale
VBM	:	Voxel-Based Morphometry
WCO	:	Wavelet Coherence
WCS	:	Wavelet Cross Spectrum
WE	:	Wavelet Energy
WEE	:	Wavelet Energy Entropy
WPLI	:	Weighted Phase Lag Index
WPS	:	Wavelet Power Spectrum

Abstract

Freezing of Gait (FOG) is a common movement disorder affecting patients with Parkinson's disease in the advanced stage. Patients often describe it as feeling like their feet are "glued to the floor" which suppresses their ability to start walking or to continue moving forward. It significantly affects patients' quality of life since the sudden and unpredictable characteristic of FOG is a common cause of falls and related injuries. It interferes with daily activities, and leads to a loss of independence. Freezing of gait is mainly perceived as an alteration in the pattern of movement, and the accelerometer, which senses movement, speed and direction, can be used as the main sensor in the detection of FOG in research studies.

Although the accelerometer has been successfully applied in the detection of FOG, it is only able to detect FOG as it occurs, which is often too late for prevention of injuries such as falls. The research in this thesis introduces electroencephalography (EEG) as a novel technique to address this problem. The EEG provides a window to see the transition episode *before* a freezing episode. Freezing of gait occurs as a result of complex, dynamic neurophysiology in the brain related to motor control as well as cognition and emotions, and the EEG signal can capture the electrical activity of the brain while this is occurring. In addition, scalp EEG has many other benefits, such as its portability, non-invasive nature, relative inexpensive cost and simple operation, whilst providing high precision in time measurements.

The study examined 16 patients (age 70.88 ± 6.92 years) with idiopathic Parkinson's disease and significant FOG, consisted of 9 patients at Hoehn and Yahr (H&Y) stages 2 and 2.5 - the early stages (56.25%), 5 patients at stage 3 - the moderate stage (31.25%), and

2 patients at stage 4 - the advanced stage (12.5%). This research studied the various features of EEG which can be used as indicators of FOG and aims to introduce the effective features as inputs for the FOG.

The first analysis was based on the classical power spectral density (extracted using Fast Fourier Transform) and its counterpart (extracted using wavelet transform). By using centroid frequency extracted from channel central zero (Cz) as input and artificial neural network as the classifier, the classification of two episodes (normal walking and 5 s transition before freezing) in the in-group was obtained with a sensitivity, specificity and accuracy of 77.0%, 74.1% and 79.5%, respectively.

The second analysis studied the cross correlation and coherence based features, aiming to improve the performance of the FOG detection and to obtain a better understanding of FOG. These features provide spatial properties of EEG which complement the time-frequency characterization gained from classical power spectral analysis.

Beyond correlation of two brain locations, in the third analysis, the brain connectivity dynamic analysis was explored further using the analysis of the causal influence between the brain locations of interest. A squared Generalized Partial Directed Coherence was used to evaluate this causal connectivity. This approach modelled effectively the inherently multivariate nature of neuronal networks. All the features were investigated with clinical EEG data. After the optimization using Independent Component Analysis and Bayesian regularization, and applying squared Generalized Partial Directed Coherence connectivity estimation, in the in-group the classifier achieved a sensitivity, specificity and accuracy of 89.1%, 91.2%, and 90.2% , respectively. The results in the out-group were relatively similar with a sensitivity, specificity and accuracy of 86.5%, 92.8% and 89.5%, respectively.

In addition, the physiology analysis provided the characterization of FOG. Beta oscillations in central lead were found to underlie the neural activity in transition to the freezing episode in power spectral measurement. In coherence study, pairwise frontocentral showed significant change, especially in the theta frequency. Effective connectivity also showed significant alteration on the causality measurement in this area. This finding lead

to the development of the predicted mechanism underlying FOG.

In summary, the techniques proposed in this dissertation contribute to the development of the detection system of FOG that can be used by patients with PD to improve their symptoms with satisfactory classification performance. In addition, the results of the experiment provide the electrophysiological signature of FOG in PD lead to novel insights into the pattern of spatiotemporal dynamic of the brain underlying this debilitating symptom of PD.